

## MELANOMA WITH REGRESSION AND IN-TRANSIT METASTASIS

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### Abstract

**Introduction.** Melanoma is an aggressive tumor with an increasing incidence worldwide. In-transit metastases represent a unique pattern of dissemination.

**Case report.** We report the case of a 42-year-old woman who presented with two lesions on the left latero-cervical region: a pigmented macule with irregular borders and colors and a firm, dome-shaped 5 mm nodule with an erythematous base and a black crust on top, at the periphery of the first lesion. The clinical picture supported the diagnosis of melanoma with in-transit metastasis, but the histopathology examination raised, initially, the problem of two primary melanomas: a superficial spreading melanoma and a minimal deviation melanoma.

**Conclusions.** Our case highlights the necessity of clinical and histopathological correlations in every case and the necessity of a good collaboration between the dermatologist and the pathologist.

**Keywords:** melanoma, regression, metastasis, in-transit

### Introduction

Melanoma is the most life-threatening form of skin cancer, with an increasing incidence worldwide (3.1% per year) [1]; in Europe the incidence rate is 11.1/100000 and the mortality rate 2.3/100000 [2]. The incidence rates are rising faster than for other types of malignancy [3], melanoma being a socio-economic burden.

It has an unpredictable behavior with an increased ability to metastasize [4], frequently via lymphatic vessels. In-transit metastases are defined as cutaneous metastases found in the dermis or subcutaneous tissue between the primary melanoma and the draining lymph node basin and are thought to be due to the involvement of the dermal and subdermal lymphatics. The incidence of in-transit metastases is less than 10% [5], and this event can be present synchronous with the primary melanoma or can

appear after the excision of the tumor.

Melanoma is also one of the most immunogenic solid cancers, and the immune response of patients with melanoma can be clinically identified as the regression of the primary tumor, this phenomenon being present 6 times more often than in other neoplasms [6]. The regression is described as a decrease of pigmentation, multiple colors, with the final step – scarring and sometimes a complete disappearance of the tumor. Dermoscopic, the features correlating with regression are scar-like depigmentation, pink coloration of the background, linear-irregular vessels, globular pattern of the vessels, remnants of pigmentation and a peppering aspect [7]. Histologically the regression is identified when there is a partial or complete absence of tumor cells, accompanied by lymphocytic infiltrate, melanophages, fibrosis and telangiectasia [7]. It is a frequent finding in cutaneous melanoma, the rate reported in the literature being 10-35% [8].

We report one unusual presentation of melanoma

with regression and with an in-transit nodular and amelanotic metastasis which raised initially the problem of differentiation from minimal deviation melanoma. An informed consent was signed by the patient for her data and pictures to be used for scientific purpose.

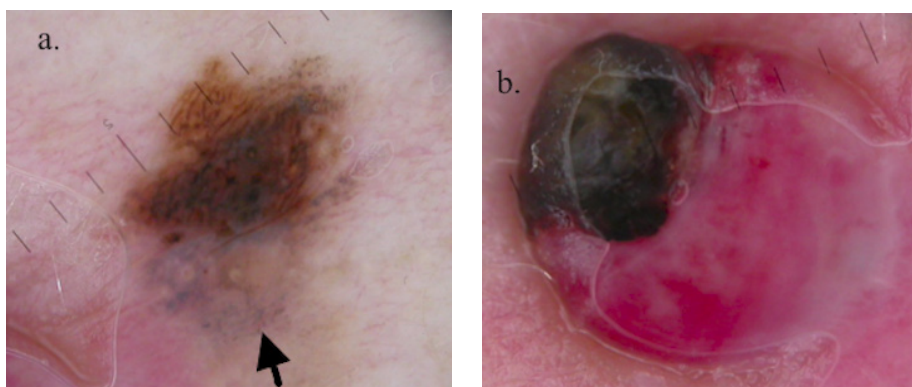
### Case Report

A 42-year-old woman presented with a pigmented lesion on the left latero-cervical region. The lesion was noticed there for a long period of time as a brown spot which started to grow four years before the presentation. In the last six months a nodule grew at the periphery of the pigmented lesion, then the brown pigment between the macular part and the nodular one began to fade. It was a melanocytic lesion – a 5 mm asymmetric, hyperpigmented macule, with irregular borders and colors and nearby a firm, dome-shaped 5 mm nodule with an erythematous base and a black crust on top (Figure 1). Dermoscopic examination revealed atypical pigmented network, brown-black

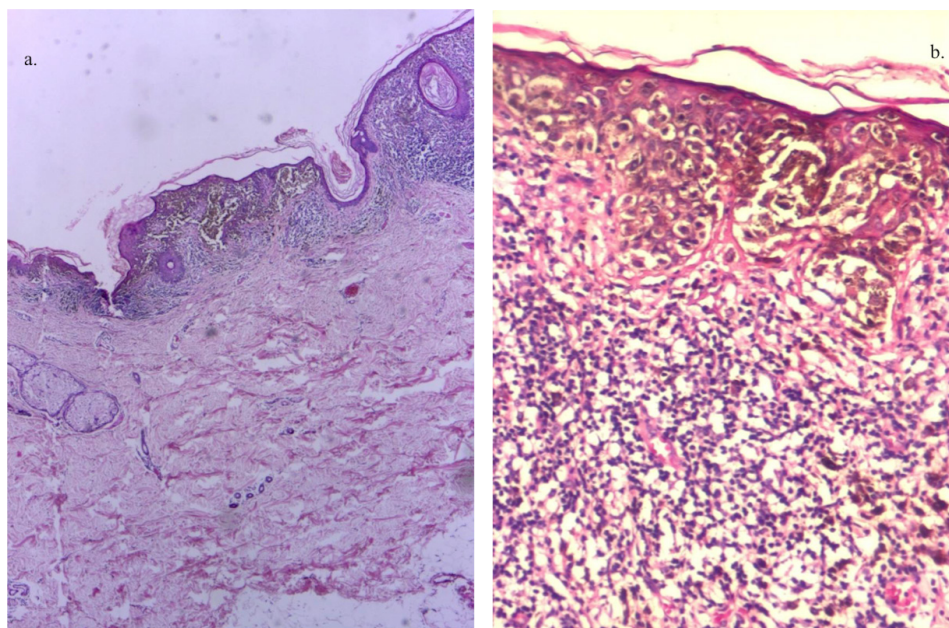
globules, pink coloration of the background and peppering, corresponding to the pigmented lesion. The nodular lesion showed milky-red area covered partially by a whitish veil, and a black structureless area at the periphery (Figure 2 a,b). The clinical picture together with the history of the lesion supported the diagnosis of superficial spreading melanoma with in-transit amelanotic metastasis. The lesion was excised and the histopathologic evaluation revealed a 0.5 mm thickness, Clark level II, non-ulcerated, moderately pigmented, superficial spreading melanoma with a mitotic rate less than 1 mitosis/mm<sup>2</sup> with important inflammatory infiltrate and melanophages – suggestive for regression; the nodular part was an expansive proliferation with small monomorphic cells with necrosis and an increased mitotic activity – changes indicating a cutaneous metastasis (Figure 3, 4). The sentinel lymph node biopsy was negative. Complementary tests (regional lymph node ultrasonography, head and neck CT) ruled out distant metastases.



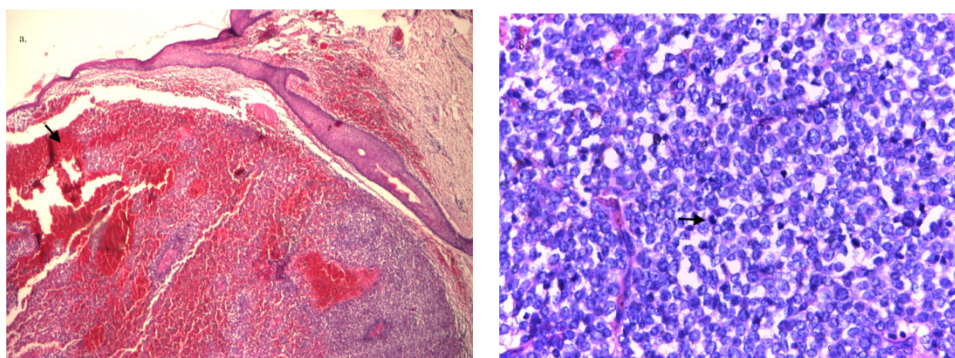
**Figure 1.** Clinical picture – primary superficial spreading melanoma (upper lesion) with in-transit amelanotic metastasis (lower lesion).



**Figure 2.** Dermoscopy – a. Primary melanoma: atypical pigmented network, brown-black globules, peppering (arrow); b. Metastatic nodule: milky-red area with whitish veil and a black structureless area at the periphery.



**Figure 3.** Histopathological picture of the primary melanoma (HE stain 4X-a, 10X-b) – a. tumoral cells with moderate pigmentation, fibrosis in the dermis; b. pagetoid cells, inflammatory infiltrate.



**Figure 4.** Histopathological picture of the metastatic nodule (HE stain 2X-a, 40X-b) – a. an expansive proliferation with necrosis (arrow); b. small monomorphic cells with an increased mitotic activity (arrow).

## Discussion

Cutaneous metastases often occur when melanoma progresses [9], the skin being the site of secondary lesions in 2-20% cases [10]. The 5-year survival rates in patients with loco-regional metastases are between 39% and 70% [11]. The AJCC reported a 5-year survival rate of 69%, in patients with intralymphatic metastases in the absence of nodal metastases, and 46% when the regional lymph nodes were affected [11]. Weide et al. conducted a study in patients with in-transit or satellite metastases and proved that the most important prognostic factor for stage III melanoma patients with skin in-transit or satellite metastases was the involvement of the lymph nodes. Another unfavorable prognostic factor was the tumor thickness of the primary lesion. From the study group, 34.5% patients had synchronous primary melanoma and loco-regional cutaneous metastases, but there was no difference in the

survival rates between these patients with skin metastases present at the time of the excision, patients with stage I/II with progressive disease or patients with unknown primary melanoma and skin metastases [12].

Our case had a thin superficial spreading melanoma with synchronous in-transit metastasis, but without lymph nodes involvement, these being factors in favor of a good prognosis, as stated by Weide et al. [12].

Another histopathologic feature found in our case, but with an unclear prognostic significance, was the regression. Several studies have described regression as a negative prognostic factor, because it may lead to an underestimation of the initial thickness of melanoma. It had been proposed as a potential marker of dissemination, being associated with a poor prognosis [13,14]. Shaw et al. assumed that the presence of metastases in the lymph nodes might determine an immune reaction which could



lead to the regression of the melanoma cells [15]. But in our case the regression was present, despite the absence of the lymph nodes involvement, supporting the idea stated in other studies that regression might be a favorable prognostic factor, even after a negative sentinel lymph node biopsy [16,17].

The particularity of our case was the histology of in-transit metastases, which reminded of a minimal deviation melanoma. Minimal deviation melanoma was described as a group of lesions that resemble acquired melanocytic nevi or Spitz nevi, but their growth pattern is different – it is expansive and looks like a vertical growth phase [18]. Therefore minimal deviation melanoma shares histological and cytological features of both melanomas and melanocytic nevi, being a distinct clinical-pathologic entity, which accounts for 1-3% of the melanoma cases [19]. McNutt et al. have shown that some metastases may have a nevoid phenotype, a clinical-pathologic correlation being required to differentiate them from a primary melanoma or from a nevus [20]. In our case, even though the histology of the nodular lesion resembled a minimal deviation melanoma, the clinical aspect and the history were suggestive for a metastasis.

### Conclusion

Our case supports the unpredictable behavior of melanoma and illustrates the challenge in establishing the correct diagnosis of this tumor, which could lead to appropriate management of the disease. Based only on histopathological examination, the lesions could have been interpreted as two different melanomas, but the history, the clinical and the dermoscopy examination were in favor of a melanoma with regression and in-transit metastasis. This emphasizes the necessity of clinical and histopathological correlations in every case and the necessity of a good collaboration between the dermatologist and the pathologist.

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